General

Guideline Title

Diagnosis and management of colorectal cancer. A national clinical guideline.

Bibliographic Source(s)

Scottish Intercollegiate Guidelines Network (SIGN). Diagnosis and management of colorectal cancer. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2011 Dec. 56 p. (SIGN publication; no. 126). [211 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Scottish Intercollegiate Guidelines Network (SIGN). Management of colorectal cancer. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2003 Mar. 47 p. (SIGN publication; no. 67). [256 references]

Any amendments to the guideline will be noted on the Scottish Intercollegiate Guidelines Network (SIGN) Web site .

Recommendations

Major Recommendations

Note from the Scottish Intercollegiate Guidelines Network (SIGN) and National Guideline Clearinghouse (NGC): In addition to these evidence-based recommendations, the guideline development group also identifies points of best clinical practice in the full-text guideline document.

The grades of recommendations (A-D) and levels of evidence (1++, 1+, 1-, 2++, 2+, 2-, 3, 4) are defined at the end of the "Major Recommendations" field.

Key Recommendations

The following recommendations were highlighted by the guideline development group as the key clinical recommendations that should be prioritised for implementation. The grade of recommendation relates to the strength of the supporting evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

Primary Care and Referral

B - Patients over the age of 40 who present with new onset, persistent or recurrent rectal bleeding should be referred for investigation.

C - Review of the patient by a regional clinical genetics service is recommended for accurate risk assessment if family history of colorectal cancer is the principal indication for referral for investigation.

B - All symptomatic patients should have a full blood count. In cases of anaemia the presence of iron deficiency should be determined.

Diagnosis

D - Colonoscopy is recommended as a very sensitive method of diagnosing colorectal cancer, enabling biopsy and polypectomy.

C - Computed tomography (CT) colonography can be used as a sensitive and safe alternative to colonoscopy.

Surgery

C - Mesorectal excision is recommended for rectal cancers where the patient is fit for radical surgery. The mesorectal excision should be total for tumours of the middle and lower thirds of the rectum, and care should be taken to preserve the pelvic autonomic nerves wherever this is possible without compromising tumour clearance.

C - When an abdominoperineal excision of the rectum is required for very low rectal cancers which cannot be adequately excised by a total mesorectal excision, then an extralevator approach to abdominoperineal excision of the rectum is recommended.

Pathology

B - All reporting of colorectal cancer specimens should be done according to, or supplemented by, the Royal College of Pathologists' minimum data set.

Chemotherapy and Radiotherapy

A - All patients with Stage III colorectal cancer should be considered for adjuvant chemotherapy.

Follow Up

A - Patients who have undergone curative resection for colorectal cancer should undergo formal follow up in order to facilitate the early detection of metastatic disease.

Prevention and Screening

Diet and Excess Weight

Weight

D - Maintaining a body mass index (BMI) close to the lower end of the normal range is advised for the general population to reduce the risk of developing colorectal cancer.

Diet

D - The general population should be advised to:

- Eat at least five portions (400 g or 14 oz) of non-starchy vegetables and fruits each day and to eat relatively unprocessed cereal with every meal
- Keep consumption of red meat to less than 500 g (18 oz) per week and avoid processed meat.

Alcohol

D - The general population should be advised that if alcoholic drinks are consumed they should be limited to no more than two drinks (four units) per day for men and one drink (two units) per day for women.

Smoking

B - The population of Scotland should be encouraged not to smoke, citing decreased colorectal cancer risk as one of the reasons.

Physical Activity

D - Physical activity of at least moderate intensity (equivalent to brisk walking) for a minimum of 30 minutes five days a week is recommended for the whole population (unless contraindicated by a medical condition).

Hormone Therapy

B - The use of hormone replacement therapy specifically to prevent colorectal cancer is not recommended.

Screening

Population Screening

A - Population screening for colorectal cancer using the guaiac faecal occult blood testing (FOBT) should continue in the Scottish population until further evidence on other modalities is available.

Screening and Surveillance of Patients with Inflammatory Bowel Disease

D - All patients with ulcerative colitis or Crohn's colitis of 10 years duration should undergo a screening colonoscopy.

D - Chromoendoscopy with pan-colonic dye-spraying and targeted biopsy of abnormal areas is advised for detecting dysplasia. If chromoendoscopy is not used, 2-4 random biopsies should be taken from every 10 cm of the colon, in addition to biopsies of any suspicious areas.

D - Surveillance colonoscopies should be performed yearly, 3-yearly or 5-yearly according to risk stratification.

D - Colectomy should be performed for high-grade dysplasia, cancer, any dysplasia-associated lesion/mass that cannot be entirely resected endoscopically, and low-grade dysplasia confirmed by two expert gastrointestinal pathologists.

See Table 1 in the original guideline document for optimal surveillance intervals for patients with inflammatory bowel disease.

Surveillance of Patients After Removal of Adenomatous Polyps

D - Patients who have undergone colonoscopic polypectomy for adenomas should be offered follow-up colonoscopy based on risk stratification.

D - Patients with one or two adenomas <1 cm in size without high-grade dysplasia are at low risk and only require follow-up colonoscopy at five years if other factors indicate the need for further surveillance. If no polyps are found, further surveillance is not required.

D The presence of either 3-4 small adenomas (<1 cm), or one adenoma >1 cm in size confers an intermediate risk, and surveillance colonoscopy should be undertaken at three years. If surveillance colonoscopy is subsequently normal on two consecutive occasions, it may cease.

D - Patients with ≥5 small adenomas, or ≥3 adenomas with at least one polyp ≥1 cm in size are at high risk, and should undergo colonoscopy at one year.

<u>The Impact of Colorectal Cancer on Patients and Their Families</u>

Interventions to Alleviate the Impact of Colorectal Cancer

D - Information about local support services should be made available to both the patient and their relatives.

B - Clinicians must be aware of the potential for physical, psychological, social and sexual problems after all colorectal cancer surgery, including sphincter-saving operations.

Methods and Sources of Communication

B - Listening and explaining skills can be improved by high-quality courses, and all healthcare professionals in cancer care should undergo such training.

B - Healthcare professionals in cancer care should consider giving either written summaries or recordings of consultations to people who have expressed a preference for them.

Involving the Patient in the Decision-Making Process

D - Healthcare professionals should respect patients' wishes to be involved when making plans about their own management.

D - Patients should be given clear information about the potential risks and benefits of treatment, in order that they can make choices.

<u>Genetics</u>

B - Individuals at risk or known to be carrying a colorectal cancer (CRC) syndrome gene mutation should be offered colonic screening according to The British Society of Gastroenterology (BSG) and the Association of Coloproctology for Great Britain and Ireland (ACPGBI) guidelines.

See Tables 2 and 3 in the original guideline document for summaries of BSG/ACPGBI recommendations for colorectal cancer screening and surveillance in moderate risk and high risk family groups, respectively.

D - Family history should be used to inform decision making about colonoscopic screening in asymptomatic individuals.

B - All individuals whose family history is suggestive of a CRC syndrome should be referred to a clinical genetics service for consideration of genetic testing to clarify the risk.

Primary Care and Referral

B - Patients over the age of 40 who present with new onset, persistent or recurrent rectal bleeding should be referred for investigation.

D - For patients under the age of 40 with low-risk features and transient symptoms a watch and wait policy is recommended.

C - Review of the patient by a regional clinical genetics service is recommended for accurate risk assessment if family history of colorectal cancer is the principal indication for referral for investigation.

B - General practitioners should perform an abdominal and rectal examination on all patients with symptoms indicative of colorectal cancer. A positive finding should expedite referral, but a negative rectal examination should not rule out the need to refer.

B - All symptomatic patients should have a full blood count. In cases of anaemia the presence of iron deficiency should be determined.

B - All patients with unexplained iron deficiency anaemia should be referred for endoscopic investigation of upper and lower gastrointestinal tracts.

Diagnosis

Endoscopy

D - Colonoscopy is recommended as a very sensitive method of diagnosing colorectal cancer, enabling biopsy and polypectomy.

Radiological Diagnosis

C - CT colonography can be used as a sensitive and safe alternative to colonoscopy.

D - Minimal preparation CT is an alternative to CT colonography in frail elderly patients.

Initial Staging

D - All patients with colorectal cancer should be staged by contrast enhanced CT of the chest, abdomen and pelvis unless the use of intravenous iodinated contrast is contraindicated.

C - Magnetic resonance imaging (MRI) of the rectum is recommended for local staging of patients with rectal cancer.

C - Endoluminal ultrasound (US) can be used in a complementary role with MRI in staging patients with early rectal cancer.

Positron Emission Tomography (PET)

C - In patients with apparently organ-restricted liver or lung metastases (either at primary presentation or during follow up) who are being considered for resection, a PET/CT scan should be considered prior to the administration of cytoreductive chemotherapy. The identification of occult metastatic disease prior to resection or chemotherapy may render resection inappropriate or may alter patient's management.

D - Fluoro-deoxy-glucose (FDG) PET/CT should be used in the evaluation of patients with raised tumour marker carcinoembryonic antigen (CEA) with negative or equivocal conventional imaging or assessment of possible pelvic recurrence and pre-sacral mass following treatment.

Surgery

Preoperative Staging

C - Complete colonic examination by colonoscopy, CT colonography or barium enema should be carried out, ideally preoperatively, in patients with colorectal cancer.

Preoperative Preparation

D - Patients undergoing surgery for colorectal cancer should have:

- Venous thromboembolism prophylaxis
- Antibiotic prophylaxis consisting of a single dose of antibiotics providing both aerobic and anaerobic cover given within 30 minutes of induction of anaesthesia.

B - Preoperative mechanical bowel preparation is recommended for patients undergoing restorative rectal resection.

Perioperative Blood Transfusion

B - If a patient undergoing colorectal cancer surgery is deemed to require a blood transfusion, this should not be withheld on account of a possible association with increased risk of cancer recurrence.

Techniques in Colorectal Cancer Surgery

Rectal Cancer

C - Mesorectal excision is recommended for rectal cancers where the patient is fit for radical surgery. The mesorectal excision should be total for tumours of the middle and lower thirds of the rectum, and care should be taken to preserve the pelvic autonomic nerves wherever this is possible without compromising tumour clearance.

C - When an abdominoperineal excision of the rectum is required for very low rectal cancers which cannot be adequately excised by a total mesorectal excision, then an extralevator approach to abdominoperineal excision of the rectum is recommended.

Colon Cancer

C - It is recommended that colon cancer is treated with radical surgery involving complete mesocolic excision and flush ligation of the colonic vessels.

Anastomoses

C - With a low rectal anastomosis, consider giving a defunctioning stoma.

C - With a low rectal anastomosis after total mesorectal excision (TME), consider a colopouch.

B - After a low rectal anastomosis (i.e., after a TME) a defunctioning stoma should be constructed unless there are compelling reasons not to do so.

Local Excision of Colorectal Cancers

C - The relative risks of operative morbidity and recurrence must be carefully weighed and explained fully to the patient so that an informed decision can be made regarding local excision and rectal cancer.

C - Further surgery for pedunculated polyp cancers that have been removed endoscopically is indicated if:

- There is histological evidence of tumour at, or within 1 mm of, the resection margin
- There is lymphovascular invasion
- The invasive tumour is poorly differentiated

Laparoscopic Surgery for Colorectal Cancer

A - Laparoscopic and open surgery can be offered for resection of colorectal cancer.

Management of Malignant Colonic Obstruction

C - Mechanical large bowel obstruction should be distinguished from pseudo-obstruction before surgery.

C - Patients with malignant obstruction of the large bowel should be considered for immediate resection.

A - If immediate reconstruction after resection is deemed feasible, segmental resection is preferred for left-sided lesions.

B - Where facilities and expertise are available, colonic stenting can be considered for the palliation of patients with obstructing colon cancer, i.e.,

in those who are not fit for immediate resection or in those with advanced disease. The risk of colonic perforation should be taken into account.

Surgery for Advanced Disease

D - Patients with liver and lung metastases should be considered for resection or, in the case of liver disease, in situ ablation.

D - In patients with advanced local or recurrent disease, careful consideration should be given to surgical excision or palliative intraluminal procedures.

Specialisation and Workload in Colorectal Cancer Surgery

B - Surgery for colorectal cancer should only be carried out by appropriately trained surgeons whose work is audited. Low rectal cancer surgery should only be performed by those trained to carry out TME.

Pathology

Important Pathological Parameters in Colorectal Cancer

B - Pathological reporting of colorectal cancer resection specimens should include information on:

- Tumour differentiation
- Staging (Dukes and tumor-node-metastasis [TNM] systems)
- Margins (peritoneal and circumferential resection margin [CRM])
- Extramural vascular invasion

Reporting in Colorectal Cancer

B - All reporting of colorectal cancer specimens should be done according to, or supplemented by, the Royal College of Pathologists' minimum data set.

Chemotherapy and Radiotherapy

Adjuvant Chemotherapy

Stage III Colorectal Cancer (T1-4 N1,2 M0)

A - All patients with Stage III colorectal cancer should be considered for adjuvant chemotherapy.

Management of Patients with Metastatic Colorectal Cancer

Resectable Liver Metastases

D - Surgical resection should be considered for all patients with resectable liver metastases.

D - Patients with resectable liver metastases should be considered for perioperative chemotherapy with a combination of oxaliplatin and fluorouracil (5-FU)/leucovorin for a total period of six months.

Unresectable Liver Metastases

D - Patients with unresectable liver metastases should be considered for downstaging chemotherapy using a combination of oxaliplatin (or irinotecan) and 5-FU/leucovorin.

First Line Chemotherapy

A - All patients with metastatic colorectal cancer should be considered for chemotherapy.

A - Combination treatment with 5-FU/leucovorin/oxaliplatin or capecitabine and oxaliplatin or 5-FU/leucovorin/irinotecan are the preferred options in patients with good performance status and organ function.

D - Consider raltitrexed for patients with metastatic colorectal cancer who are intolerant to 5-FU and leucovorin, or for whom these drugs are not suitable.

Second Line Chemotherapy

A - Second line chemotherapy should be considered for patients with metastatic colorectal cancer with good performance status and adequate organ function.

A - Irinotecan should be used as second line therapy following first line oxaliplatin (or vice versa).

Biological Therapy

B - Cetuximab should be considered in combination with 5-FU/leucovorin/oxaliplatin or 5-FU/leucovorin/irinotecan chemotherapy for patients with unresectable liver metastases if patients fulfil the Scottish Medicines Consortium (SMC) criteria. The use of cetuximab in combination with oxaliplatin and capecitabine cannot currently be recommended.

Management of Patients with Rectal Cancer

A - Patients considered to have a moderate risk of local recurrence with total mesorectal excision surgery alone, and in whom the CRM is not threatened or breached on MRI, could be considered for preoperative radiotherapy (25 Gy in five fractions over one week) and immediate TME surgery.

A - Patients who require downstaging of the tumour because of encroachment on the mesorectal fascia should receive combination chemotherapy and radiotherapy (biological effective dose [BED] >30 Gy), followed by surgery at an interval to allow cytoreduction.

Follow Up of Patients Treated for Colorectal Cancer

A - Patients who have undergone curative resection for colorectal cancer should undergo formal follow up in order to facilitate the early detection of metastatic disease.

Palliative Care and the Management of Symptoms in Advanced Disease

D - Medical measures such as analgesics, antiemetics and antisecretory drugs should be used alone or in combination to relieve the symptoms of bowel obstruction.

Definitions:

Levels of Evidence

1++: High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

1+: Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

1-: Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias

2++: High quality systematic reviews of case control or cohort studies

High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

2+: Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

2-: Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

3: Non-analytic studies, e.g., case reports, case series

4: Expert opinion

Grades of Recommendation

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A: At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or

A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

B: A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 1++ or 1+

C: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 2++

D: Evidence level 3 or 4; or

Extrapolated evidence from studies rated as 2+

Clinical Algorithm(s)

An algorithm of the Scottish referral guidelines for suspected cancer: lower gastrointestinal cancer is provided in Annex 2 of the original guideline document.

Scope

Disease/Condition(s)

- Colorectal cancer
- Hereditary non-polyposis colorectal cancer (HNPCC)
- Familial adenomatous polyposis (FAP)
- Peutz Jegher syndrome
- MUTYH-associated polyposis (MYH)
- Juvenile polyposis

Guideline Category

Counseling

Diagnosis

Evaluation

Management

Prevention

Risk Assessment

Screening

Treatment

Clinical Specialty

Colon and Rectal Surgery

Family Practice

Gastroenterology

Internal Medicine

Medical Genetics

Nursing

Oncology

Pathology

Preventive Medicine

Radiation Oncology

Radiology

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Health Plans

Hospitals

Managed Care Organizations

Nurses

Patients

Physician Assistants

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

Public Health Departments

Utilization Management

Guideline Objective(s)

- To encourage the adoption of measures in the general population and in high-risk groups to reduce the risk of developing colorectal cancer
- To promote early diagnosis in the general population and in high-risk groups
- To guide more consistent referral
- To improve all aspects of the management of patients with colorectal cancer in order to improve overall and disease-free survival and improve health-related quality of life

Target Population

- Patients in Scotland at risk for colorectal cancer
- Patients in Scotland diagnosed with colorectal cancer

Interventions and Practices Considered

Prevention/Screening

1. Diet (five or more portions of fruits and non-starchy vegetables a day, relatively unprocessed cereal with each meal, avoiding processed

meat, low red meat consumption, limiting alcohol consumption)
2. Maintaining body mass index (BMI) close to low end of normal range
3. Physical activity of moderate intensity for 30 minutes per day, 5 days per week
4. Encouragement not to smoke
5. Guaiac faecal occult blood test population screening
6. Colonoscopy with biopsy
7. Chromoendoscopy with pan-colonic dye spraying
8. Hormone therapy (not recommended)
9. Screening and surveillance intervals
10. Risk stratification

Diagnosis/Assessment

1. Family history
2. Thorough abdominal and rectal examination
3. Full blood count
4. Referral to specialist, such as clinical genetics, surgery
5. Colonoscopy
6. Radiological assessment
    - Computed tomography (CT) colonography
    - Minimal preparation CT
    - Contrast-enhanced CT of the chest, abdomen, and pelvis
    - Magnetic resonance imaging of the rectum
    - Endoluminal ultrasound
    - Fluoro-deoxy-glucose (FDG) positron emission tomography-computed tomography (PET/CT)
7. Pathological reporting of colorectal cancer resection specimens, including tumour differentiation, staging, margins, and extramural vascular invasion

Management/Treatment

1. Watch and wait (as indicated)
2. Preoperative preparation
    - Venous thromboembolism prophylaxis
    - Antibiotic prophylaxis
    - Mechanical bowel preparation
3. Surgery
    - Rectal cancer (total mesorectal excision (TME) surgery, abdominoperineal excision)
    - Colon cancer (complete mesocolic excision and flush ligation of the colonic vessels, anastomoses [colopouch, defunctioning stoma])
    - Local excision
    - Laparoscopic surgery
    - Resection or ablation of metastases
4. Management of malignant colonic obstruction
5. Adjuvant chemotherapy
6. First line chemotherapy: combination treatment with 5-flurouracil (5-FU)/leucovorin/oxaliplatin or capecitabine and oxaliplatin or 5-FU/leucovorin/irinotecan
7. Raltitrexed (for patients with metastatic colorectal cancer who are intolerant to 5-FU and leucovorin)
8. Second line chemotherapy: irinotecan following first line oxaliplatin (or vice versa)
9. Biological therapy: cetuximab in combination with 5-FU/leucovorin/oxaliplatin or 5-FU/leucovorin/irinotecan chemotherapy as indicated
10. Preoperative radiotherapy and/or chemotherapy
11. Follow-up
12. Palliative care: medical management with analgesics, antiemetics and antisecretory drugs to relieve the symptoms of bowel obstruction
13. Provision of information to patients and relatives regarding support services
14. Methods and sources for good patient communication
15. Involvement of patient in decision process

Major Outcomes Considered

- Sensitivity and specificity of diagnostic tests
- Complications from diagnostic tests
- Treatment-related morbidity and mortality
- Disease-free survival
- Relapse rate
- Overall survival
- Quality of life

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Systematic Literature Review

A systematic review of the literature was carried out using an explicit search strategy devised by the Scottish Intercollegiate Guidelines Network (SIGN) Information Officer in collaboration with members of the guideline development group. The search for systematic reviews and meta-analyses covered the Cochrane Library, MEDLINE, and EMBASE databases, from January 2002 to March 2011. The search for randomised controlled trials, cohort studies, case control studies, and cross-sectional surveys covered the Cochrane Library, MEDLINE, EMBASE, and CINAHL databases, from January 2002 to March 2011. The evidence base was updated during the course of development of the guideline, and the search was supplemented by reviewing references identified from papers from the searches and from personal databases of the guideline development group members.

Literature Search for Patient Issues

At the start of the guideline development process, a SIGN Information Officer conducted a literature search for qualitative and quantitative studies that addressed patient issues of relevance to the management of colorectal cancer. Databases searched include MEDLINE, EMBASE, CINAHL and PsycINFO, and the results were summarised and presented to the guideline development group. A copy of the MEDLINE version of the patient search strategy is available on the SIGN Web site .

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Levels of Evidence

1++: High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

1+: Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

1-: Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias

2++: High quality systematic reviews of case control or cohort studies

High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

2+: Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

2-: Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

3: Non-analytic studies, e.g., case reports, case series

4: Expert opinion

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Once papers have been selected as potential sources of evidence, the methodology used in each study is assessed to ensure its validity. The result of this assessment will affect the level of evidence allocated to the paper, which will in turn influence the grade of recommendation that it supports.

The methodological assessment is based on a number of key questions that focus on those aspects of the study design that research has shown to have a significant influence on the validity of the results reported and conclusions drawn. These key questions differ between study types, and a range of checklists is used to bring a degree of consistency to the assessment process. The Scottish Intercollegiate Guidelines Network (SIGN) has based its assessments on the MERGE (Method for Evaluating Research and Guideline Evidence) checklists developed by the New South Wales Department of Health, which have been subjected to wide consultation and evaluation. These checklists were subjected to detailed evaluation and adaptation to meet SIGN's requirements for a balance between methodological rigour and practicality of use.

The assessment process inevitably involves a degree of subjective judgement. The extent to which a study meets a particular criterion - e.g., an acceptable level of loss to follow up - and, more importantly, the likely impact of this on the reported results from the study will depend on the clinical context. To minimise any potential bias resulting from this, each study must be evaluated independently by at least two group members. Any differences in assessment should then be discussed by the full group. Where differences cannot be resolved, an independent reviewer or an experienced member of the SIGN Executive staff will arbitrate to reach an agreed quality assessment.

Evidence Tables

Evidence tables are compiled by SIGN Executive staff based on the quality assessments of individual studies provided by guideline development group members. The tables summarise all the validated studies identified from the systematic literature review relating to each key question. They are presented in a standard format to make it easier to compare results across studies, and will present separately the evidence for each outcome measure used in the published studies. These evidence tables form an essential part of the guideline development record and ensure that the basis of the guideline development group's recommendations is transparent.

Additional details can be found in the companion document titled "SIGN 50: A Guideline Developers' Handbook." (Edinburgh [UK]: Scottish Intercollegiate Guidelines Network. [SIGN publication; no. 50]), available from the SIGN Web site .

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Synthesising the Evidence

Guideline recommendations are graded to differentiate between those based on strong evidence and those based on weak evidence. This

judgement is made on the basis of an (objective) assessment of the design and quality of each study and a (perhaps more subjective) judgement on the consistency, clinical relevance and external validity of the whole body of evidence. The aim is to produce a recommendation that is evidence-based, but which is relevant to the way in which health care is delivered in Scotland and is therefore implementable.

It is important to emphasise that the grading does not relate to the importance of the recommendation, but to the strength of the supporting evidence and, in particular, to the predictive power of the study designs from which that data was obtained. Thus, the grading assigned to a recommendation indicates to users the likelihood that, if that recommendation is implemented, the predicted outcome will be achieved.

Considered Judgement

It is rare for the evidence to show clearly and unambiguously what course of action should be recommended for any given question. Consequently, it is not always clear to those who were not involved in the decision making process how guideline developers were able to arrive at their recommendations, given the evidence they had to base them on. In order to address this problem, SIGN has introduced the concept of considered judgement.

Under the heading of considered judgement, guideline development groups summarise their view of the total body of evidence covered by each evidence table. This summary view is expected to cover the following aspects:

- Quantity, quality, and consistency of evidence
- External validity (generalisability) of study findings
- Directness of application to the target population for the guideline
- Any evidence of potential harms associated with implementation of a recommendation
- Clinical impact (i.e., the extent of the impact on the target patient population, and the resources needed to treat them in accordance with the recommendation)
- Whether, and to what extent, any equality groups may be particularly advantaged or disadvantaged by the recommendations made
- Implementability (i.e., how practical it would be for the National Health Service [NHS] in Scotland to implement the recommendation)

The group are finally asked to summarise its view on all of these issues, both the quality of the evidence and its potential impact, before making a graded recommendation. This summary should be succinct, and taken together with its views of the level of evidence represent the first draft of the text that will appear in the guideline immediately before a graded recommendation.

Where no new evidence was identified to support an update, text and recommendations are reproduced verbatim from the previous version of the guideline. The original supporting evidence was not re-appraised by the current guideline development group.

Additional detail about SIGN's process for formulating guideline recommendations is provided in Section 6 of the companion document titled "SIGN 50: A Guideline Developers' Handbook." (Edinburgh [UK]: Scottish Intercollegiate Guidelines Network. [SIGN publication; no. 50], available from the SIGN Web site .

Rating Scheme for the Strength of the Recommendations

Grades of Recommendation

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A: At least one meta-analysis, systematic review, or randomised controlled trial (RCT) rated as 1++, and directly applicable to the target population; or

A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

B: A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 1++ or 1+

C: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 2++

D: Evidence level 3 or 4; or

Extrapolated evidence from studies rated as 2+

Good Practice Points: Recommended best practice based on the clinical experience of the guideline development group

Cost Analysis

The guideline developers reviewed published cost analyses.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Consultation and Peer Review

Public Consultation

The draft guideline was available on the Scottish Intercollegiate Guidelines Network (SIGN) website for a month to allow all interested parties to comment. All contributors made declarations of interest and further details of these are available on request from the SIGN Executive.

Specialist Review

This guideline was also reviewed in draft form by a group of independent expert referees, who were asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. The guideline group addresses every comment made by an external reviewer, and must justify any disagreement with the reviewers' comments. All expert referees made declarations of interest and further details of these are available on request from the SIGN Executive.

SIGN Editorial Group

As a final quality control check, the guideline is reviewed by an editorial group comprising the relevant specialty representatives on SIGN Council to ensure that the specialist reviewers' comments have been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Reduction in the risk of developing colorectal cancer in the general population and in high risk groups
- Early diagnosis of colorectal cancer in the general population and in high risk groups
- Improvement in the consistency of referral patterns

- Improvement of all aspects of the management of colorectal cancer patients in order to improve overall and disease-free survival and health-related quality of life

Potential Harms

- The majority of trials reported that the positive predictive value of guaiac faecal occult blood tests were low, which may have caused stress or anxiety for those receiving a false-positive result. The guaiac test, however, is not specific for blood which creates a problem with sensitivity and specificity.
- In a variable proportion of patients, the caecum is not reached by colonoscopy, intravenous sedation may be required, the localisation of tumour may be inaccurate, and there is a small but significant risk of complications such as bleeding, bowel perforation and death.
- Anastomotic leakage is an important and potentially fatal complication of colorectal cancer surgery, and measures to minimise it should be taken. There is no high quality evidence to support any specific technique, but a meta-analysis indicated that the only difference between hand-sewn and stapled anastomoses is a slightly increased risk of anastomotic stricture with stapling.
- Risk factors for anastomotic dehiscence are well documented and include male sex, increasing age and obesity, but in anterior resection leakage is increased with a low (<5 cm from anorectal junction) anastomosis.
- Another disadvantage of the low anastomosis is poor function, and there is good evidence from randomised trials to support the use of a colopouch in this situation.
- The risk of colonic perforation should be taken into account when stenting is used for colonic obstruction.
- Adjuvant chemotherapy for Stage II patients carries an increased risk of treatment-related morbidity and mortality associated with increasing age and comorbidity and the increased risk of relapse associated with the presence of T4 disease, high grade tumour or extramural vascular invasion. Combined treatment is more toxic than thymidylate synthase (TS) inhibition alone, which should be considered when assessing any relative advantage that it confers for Stage III patients.
- There is little good quality evidence for the use of raltitrexed in patients with metastatic colorectal cancer although there are data in the adjuvant setting and a number of phase II trials of metastatic patients which show an association between raltitrexed and an increased incidence of toxicity and treatment-related deaths.
- The long term morbidity in terms of bowel dysfunction is higher in those patients who have received preoperative radiotherapy compared to surgery alone. In a review of short course preoperative adjuvant radiotherapy 5%-13% of patients showed benefit without additional harm, 0%-2% had benefit with additional harm, 74%-87% had neither benefit nor additional harm, and 6%-11% had no benefit but additional harm.

Qualifying Statements

Qualifying Statements

- This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.
- Every care is taken to ensure that this publication is correct in every detail at the time of publication. However, in the event of errors or omissions corrections will be published in the web version of this document, which is the definitive version at all times. This version can be found on our web site www.sign.ac.uk .

Prescribing of Licensed Medicines Outwith Their Marketing Authorisation

- Recommendations within this guideline are based on the best clinical evidence. Some recommendations may be for medicines prescribed outwith the marketing authorisation (product licence). This is known as 'off label' use. It is not unusual for medicines to be prescribed outwith their product licence and this can be necessary for a variety of reasons.
- Generally the unlicensed use of medicines becomes necessary if the clinical need cannot be met by licensed medicines; such use should be

supported by appropriate evidence and experience.

- Medicines may be prescribed outwith their product licence in the following circumstances:
  - For an indication not specified within the marketing authorisation
  - For administration via a different route
  - For administration of a different dose.
- 'Prescribing medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescribers' professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines.'
- Any practitioner following a Scottish Intercollegiate Guidelines Network (SIGN) recommendation and prescribing a licensed medicine outwith the product licence needs to be aware that they are responsible for this decision, and in the event of adverse outcomes, may be required to justify the actions that they have taken.
- Prior to prescribing, the licensing status of a medication should be checked in the current version of the British National Formulary (BNF). The summary of product characteristics (SPC) should also be consulted in the electronic medicines compendium (www.medicines.org.uk).

Implementation of the Guideline

Description of Implementation Strategy

Implementation of national clinical guidelines is the responsibility of each National Health Service (NHS) Board and is an essential part of clinical governance. Mechanisms should be in place to review care provided against the guideline recommendations. The reasons for any differences should be assessed and addressed where appropriate. Local arrangements should then be made to implement the national guideline in individual hospitals, units and practices.

Key points for audit are identified in Section 14.3 of the original guideline document.

Implementation Tools

Audit Criteria/Indicators

Chart Documentation/Checklists/Forms

Clinical Algorithm

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

End of Life Care

Getting Better

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Timeliness

Identifying Information and Availability

Bibliographic Source(s)

Scottish Intercollegiate Guidelines Network (SIGN). Diagnosis and management of colorectal cancer. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2011 Dec. 56 p. (SIGN publication; no. 126). [211 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2003 Mar (revised 2011 Dec)

Guideline Developer(s)

Scottish Intercollegiate Guidelines Network - National Government Agency [Non-U.S.]

Source(s) of Funding

Scottish Executive Health Department

Guideline Committee

Not stated

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Financial Disclosures/Conflicts of Interest

All members of the guideline development group made declarations of interest and further details of these are available on request from the SIGN Executive.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Scottish Intercollegiate Guidelines Network (SIGN). Management of colorectal cancer. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2003 Mar. 47 p. (SIGN publication; no. 67). [256 references]

Any amendments to the guideline will be noted on the Scottish Intercollegiate Guidelines Network (SIGN) Web site .

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Scottish Intercollegiate Guidelines Network (SIGN) Web site .

Availability of Companion Documents

The following are available:

- Quick reference guide: Management of colorectal cancer. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2011 Dec. 2 p. Available in Portable Document Format (PDF) from the Scottish Intercollegiate Guidelines Network (SIGN) Web site .
- SIGN 50: a guideline developers' handbook. Edinburgh (UK): Scottish Intercollegiate Guidelines Network. (SIGN publication; no. 50). Available from the SIGN Web site .
- Appraising the quality of clinical guidelines. The SIGN guide to the AGREE (Appraisal of Guidelines Research and Evaluation) guideline appraisal instrument. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network, 2001. Available from the SIGN Web site .

In addition, a checklist of information to provide to patients and carers is available in section 13 and key points to audit are available in section 14 of the original guideline document .

Patient Resources

None available

NGC Status

This summary was prepared by ECRI on November 20, 2003. The information was verified by the guideline developer on January 16, 2004. The information was reaffirmed by the guideline developer in 2007 and updated by ECRI Institute on March 29, 2010. This NGC summary was updated by ECRI Institute on March 1, 2012. The updated information was verified by the guideline developer on March 8, 2012.

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